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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PAVIGLIANITI, ANTHONY JOSEPH	
ART UNIT	**PAPER NUMBER**
1626	

DATE MAILED: 03/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/784,916	VAZQUEZ ET AL.	
	Examiner	Art Unit	
	Anthony J. Paviglianiti	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,66,68-72,78,126-132,167-170 and 172* is/are pending in the application.

4a) Of the above claim(s) *68-72,127-131,168-170 and 172* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,66,78,126,132 and 167* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 66, 68 – 72, 78, 126 – 132, 167 – 170, and 172 are currently pending in the application. Applicant's preliminary amendment of August 18, 2004, has been entered; accordingly, **Claims 2 – 65, 67, 73 – 77, 79 – 125, 133 – 166, 171, and 173** were cancelled by that amendment prior to examination.

Priority

This application is a Continuation application of Application # 10/237,184 filed September 9, 2002 (now U.S. Patent 6,727,282), which is a Continuation application of Application # 09/884,462 filed June 20, 2001 (now U.S. Patent 6,469,207), which is a Continuation application of Application # 09/419,816 filed October 18, 1999 (now U.S. Patent 6,313,345), which is a Continuation application of Application # 09/041,016 filed March 12, 1998 (now U.S. Patent 6,022,994), which is a Continuation application of Application # 08/541,747 filed October 10, 1995 (now U.S Patent 5,760,076), which is a Divisional application of Application # 08/110,912 filed August 24, 1993 (now U.S. Patent 5,463,104), which is a Continuation-in-Part application of Application # 07/935,490 filed August 25, 1992, which was abandoned.

The pending application does not claim benefit to a foreign priority document or to a Provisional application.

Information Disclosure Statement

The Information Disclosure Statements filed on February 24, 2004, August 18, 2004, and August 25, 2004, are hereby acknowledged and were considered by the examiner.

Election/Restrictions

The Markush groups set forth in the claims include both independent and distinct inventions, and patentably distinct compounds (or species) within each invention. However, this application discloses and claims a plurality of patentably distinct inventions far too numerous to list individually. Moreover, each of these inventions contains a plurality of patentably distinct compounds, also far too numerous to list individually. **For these reasons provided below, restriction to one of the following inventions is required under 35 U.S.C. 121,** wherein an Invention is a set of patentably distinct inventions of a broad statutory category (e.g., compounds, methods of use, methods of making, etc.):

I. **Claims 1, 66, 78, 126, 132, and 167**, drawn to chemical compounds and compositions having structures depicted in Claim 1 (as amended), Claim 78 (as amended) and Claim 132 (as amended), classified in class 564, subclasses 89 and 93; class 544, subclasses 110, 159; Class 546, subclasses 335, 336; Class 549, subclasses 65, 75, and other subclasses.

II. **Claims 68, 69, 70 – 72, 127 – 131, 168 – 170, and 172**, drawn to methods of using compounds and compositions having structures depicted in Claim 1 (as amended), Claim 78 (as amended) and Claim 132 (as amended), classified in classes 514, subclasses 237.8, 357, 438, 533, 539, and other subclasses.

In addition to an election of one of the above Groups, restriction is further required under 35 U.S.C. §121 as follows:

In accordance with the decisions in In re Harnisch, 631 F.2d 716, 206 USPQ 300 (CCPA 1980) and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App & Int. 1984), restriction of a

Markush group is proper where the compounds with the group either (1) do not share a common utility, or (2) do not share a substantial structural feature disclosed as being essential to that utility. In addition, a Markush group may encompass a plurality of independent and distinct inventions where two or more members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the claim obvious under 35 U.S.C. §103 with respect to the other member(s).

If **Group I or Group II** is elected, **an election of a single compound is further required**, including an exact definition of each substitution on the base molecule, where a single member at each substituent group is selected. If the base molecule has variable groups [in order of appearance] $\mathbf{R^1}$, $\mathbf{R^2}$, **X**, **X'**, **Y**, **Y'**, **x**, **t**, $\mathbf{R^3}$, $\mathbf{R^{17}}$, $\mathbf{R^{15}}$, $\mathbf{R^4}$, $\mathbf{R^6}$, $\mathbf{R^{30}}$, $\mathbf{R^{31}}$, $\mathbf{R^{32}}$ $\mathbf{R^{33}}$, $\mathbf{R^{34}}$ where, for example, $\mathbf{R^3}$ is recited to represent:

> "...hydrogen, haloalkyl, alkenyl, alkynyl, hydroxyalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heteroaryl, heterocycloalkylalkyl, aryl, aralkyl, heteroaralkyl, aminoalkyl and mono- and disubstituted aminoalkyl radicals, wherein said substituents are selected from alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, and heterocycloalkylalkyl radicals, or in the case of a disubstituted aminoalkyl radical, said substituents along with the nitrogen atom to which they are attached form a heterocycloalkyl or a heteroaryl radical,"

then Applicant must select a single substituent representing $\mathbf{R^3}$, such as "isopentyl," and so on, such that there are specific values representing each subsequent variable position, so that a single compound is identified. One suggestion for the election of a single compound is to select one of the compounds in Tables 1 – 9 in the Specification at pp. 39 - 63.

In the instant case, upon election of a single compound, the Office will review the claims and disclosure to determine the scope of the independent invention encompassing the elected

compound (compounds which are so similar as to be within the same inventive concept and reduction to practice). The scope of an independent invention will encompass all compounds within the scope of the claim which fall into the same class and subclass as the elected compound, but may also include additional compounds which fall in related subclasses.

Examination will then proceed on the elected compound *and* the entire scope of the invention encompassing the elected compound as defined by common classification. A clear statement of the examined invention, defined by those class(es) and subclass(es) will be set forth in the first action on the merits.

Note that the restriction requirement will not be made final until such time as Applicant is informed of the full scope of compounds along with (if appropriate) the process of using or making the compounds under investigation. This will be set forth by reference to specific class(es) and subclass(es) examined.

Should Applicant traverse on the ground that the compounds are not patentably distinct, Applicant should submit evidence or identify such evidence now of record showing the compounds to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. §103(a) of the other invention.

All compounds falling outside of the class(es) and subclass(es) of the selected compound and any other subclass encompassed by the election above will be directed to non-elected subject matter and will be withdrawn from consideration under 35 U.S.C. §121 and 37 C.F.R. §1.142(b). Applicant may reserve the right to file divisional applications on the remaining subject matter.

The provisions of 35 U.S.C. §121 apply with regard to double patenting covering divisional applications.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. §1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 C.F.R. §1.48(b) and by the fee required under 37 C.F.R. §1.17(i).

If desired upon election of a single compound, applicants can review the claims and disclosure to determine the scope of the invention and can set forth a group of compounds which are so similar within the same inventive concept and reduction to practice. Markush claims must be provided with support in the disclosure for each member of the Markush group. See MPEP §608.01(p). Applicant should exercise caution in making a selection of a single member for each substituent group on the base molecule to be consistent with the written description.

Rationale Establishing Patentable Distinctiveness Within Each Group

Each Group listed above is directed to or involves the use of compounds which are recognized in the art as being distinct from one another because of their diverse chemical structure, their different chemical properties, modes of action, different effects and reactive conditions (MPEP §806.04, MPEP §808.01). Additionally, the level of skill in the art is not such that one invention would be obvious over the other invention (Group); i.e., they are patentable over each other. Chemical structures which are similar are presumed to function similarly, whereas chemical structures that are not similar are not presumed to function similarly. The presumption even for similar chemical structures though is not irrebuttable, but may be

overcome by scientific reasoning or evidence showing that the structure of the prior art would not have been expected to function as the structure of the claimed invention. Note that in accordance with the holding of Application of Papesch, 50 CCPA 1084, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) and In re Lalu, 223 USPQ 1257 (Fed. Cir. 1984), chemical structures are patentably distinct where the structures are either not structurally similar, or the prior art fails to suggest a function of a claimed compound would have been expected from a similar structure.

The above Groups represent general areas wherein the inventions are independent and distinct, each from the other, because of the following reasons:

Group I and **Group II** are related as product and method of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially-different process of using that product. See MPEP §806.05(h). Applying this rule to the instant case, the method of treating an HIV infection (e.g., **Claim 71** in **Group II**) can be practiced with another materially-different product, such as saquinavir (also an HIV-protease inhibitor). See, e.g., A. Collier, et al., "Treatment of Human Immunodeficiency Virus Infection with Saquinavir, Zidovudine, and Zalcitabine," N. Engl. J. Med., vol. 334(16), pages 1011 – 1017, at p. 1015, col. 1, lines 33 – 36.

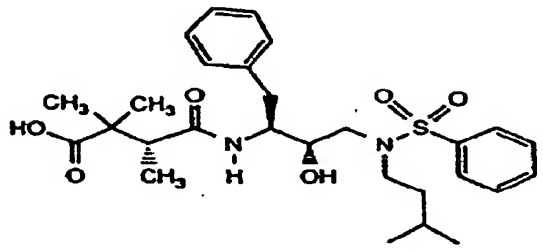
In addition, because of the plethora of classes and subclasses in each of the Groups, a serious burden is imposed upon the examiner to perform a complete search of the defined areas. Therefore, for the reasons given above, the restriction set forth is proper, and not to restrict would impose a serious burden in the examination of this application.

Advisory of Rejoinder

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

During a telephone conversation with Joseph Skerpon, Esq., on February 10, 2005, the above restriction requirements were discussed, and **a provisional election was made of Group I and of the compound** [1S-[1R*(S*),2S*]]-4-[[2-hydroxy-3-[(3-methylbutyl) (phenyl-sulfonyl)amino]-1-(phenylmethyl)propyl]amino]-2,2,3-trimethyl-4-oxo-butanoic acid (Compound #2 in Table 8, p. 61 of the Specification), which has the structure



The election was made "with traverse," on the basis that claims for chemical compounds and methods represent a single invention because chemical compounds are required to have utility.

Applicant is advised that the reply to this requirement to be complete must include an election of the Invention to be examined even though the requirement be traversed. 37 C.F.R. §1.143.

Applicant is further advised that a reply to this requirement must include an identification of the specific compound that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Response to Election "With Traverse"

The above election by Applicant was made "with traverse," on the basis that the products (**Group I**) and their methods of use (i.e., **Group II**) represent a single invention because chemical compounds are required to have utility, and therefore ought not to be restricted. Upon reconsideration of the issue, the examiner believes that the restriction between the products and methods of use is proper, for the following three reasons:

(1) the two inventions (Groups) were shown to be "distinct" inventions pursuant to MPEP §806.05(h) in the analysis presented earlier in this action.

(2) the base molecule for the products claims contains a large number of variables [$\mathbf{R^1}$, $\mathbf{R^2}$, **X**, **X'**, **Y**, **Y'**, **x**, **t**, $\mathbf{R^3}$, $\mathbf{R^{17}}$, $\mathbf{R^{15}}$, $\mathbf{R^4}$, $\mathbf{R^6}$, $\mathbf{R^{30}}$, $\mathbf{R^{31}}$, $\mathbf{R^{32}}$ $\mathbf{R^{33}}$, $\mathbf{R^{34}}$] which represent a broad array of entities, which yields products of widely-divergent classifications. For example, $\mathbf{R^3}$ represents

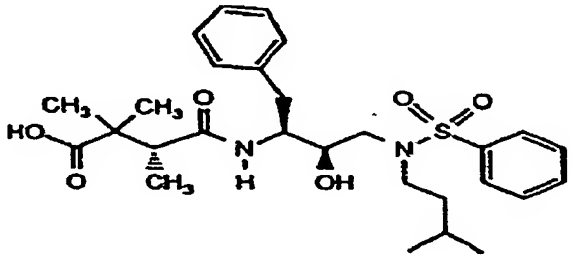
"...hydrogen, haloalkyl, alkenyl, alkynyl, hydroxyalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heteroaryl, heterocycloalkylalkyl, aryl, aralkyl, heteroaralkyl, aminoalkyl and mono- and disubstituted aminoalkyl radicals, wherein said substituents are selected from alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, and heterocycloalkylalkyl radicals, or in the case of a disubstituted aminoalkyl radical, said substituents along with the nitrogen atom to which they are attached form a heterocycloalkyl or a heteroaryl radical," and $\mathbf{R^{33}}$ and $\mathbf{R^{34}}$ can each be the same radicals as listed for $\mathbf{R^3}$, as well as some additional combinations. Without restriction, the plethora of classes and subclasses in each of the Groups would impose a serious burden upon the examiner to perform a complete search of the defined areas to examine the application.

(3) the "Advisory of Rejoinder" (see above) was discussed with Applicant, and provides that provides that, in the event that the elected product claims are found to be allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP §821.04, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR §1.104. For the reasons noted above, withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. The rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. §§ 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained.

Therefore, the restriction requirement between **Group I** and **Group II** is proper at this stage of examination, and is maintained in this Office Action over the traverse by Applicant.

Status of Claims

The art that was searched for examination of this application was (1) the elected species, [1S-[1R*(S*),2S*]]-4-[[2-hydroxy-3-[(3-methylbutyl) (phenylsulfonyl)amino]-1-(phenylmethyl)propyl]amino]-2,2,3-trimethyl-4-oxo-butanoic acid (Compound #2 in Table 8 on p. 61 of the Specification), which has the structure



(2) the art in class 564, subclasses 89 and 93, and class 544, subclass 110; and (3) a search of the generic structure in as depicted in Claim 1 (as amended). However, a search of the prior and co-pending applications by the inventors showed that the elected compound had been previously patented by the same inventive entity, as described below.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ormum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness are summarized as follows:

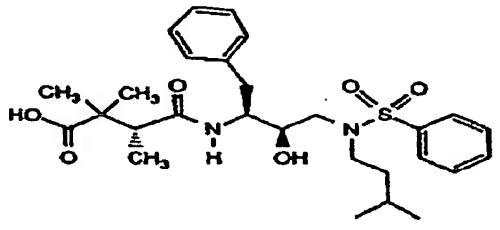
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The Graham factors will be applied below.

Double patenting with U.S. Patent No. 5,463,104

Double patenting – the "elected" compound:

The "elected" compound by Applicant, namely [1S-[1R*(S*),2S*]]-4-[[2-hydroxy-3-[(3-methylbutyl) (phenylsulfonyl)amino]-1-(phenylmethyl)propyl]amino]-2,2,3-trimethyl-4-oxo-butanoic acid (Compound #2 in Table 8 on p. 61 of the Specification), which has the structure



, is rejected under the judicially created doctrine of

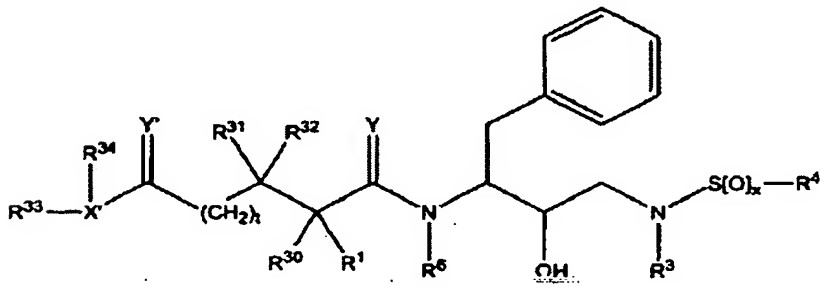
obviousness-type double patenting as being unpatentable over Claim 14 of U.S. Patent No. 5,463,104 at col. 59, lines 2 – 5 (the third-listed compound), in which this particular compound was previously patented by these inventors and assignee.

Double patenting – Claims 1 and 66:

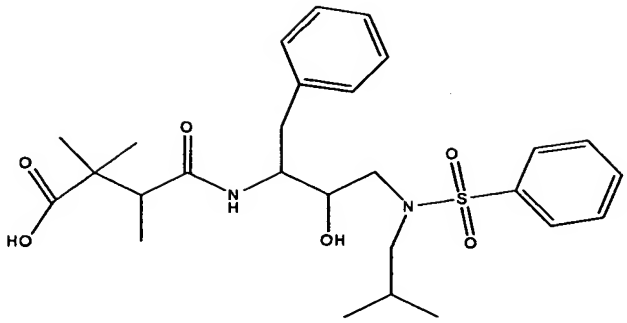
Claim 1 (compound) and **Claim 66** (composition of compound of Claim 1 and a carrier) of the instant application are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1, 2, 3, 4, and 14 of U.S. Patent No. 5,463,104. The prior patent was issued to the same inventors and assignee as the present application. Although the conflicting claims are not identical, they are not patentably distinct from each other because the chemical compounds claimed in U.S. Patent No. 5,463,104 fully encompass the compounds and compositions in **Claims 1 and 66** of the present application.

Determining the scope and content of the prior art

Claim 1 of the present application discloses compounds of the following structure:

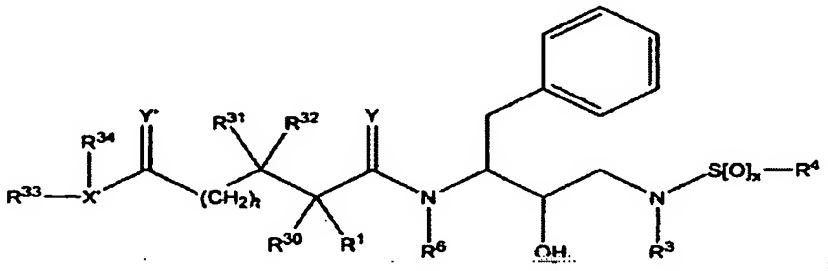


U.S. Patent No. 5,463,104 discloses fifteen chemical compounds which fully anticipate the genus structure in **Claim 1** of the present application. (See "Claim 14" of U.S. Patent No. 5,463,104, col. 58, line 61 – col. 59, line 46). The chemical structure of one of those fifteen species (corresponding to the "elected" compound) was already shown in the preceding section. Another

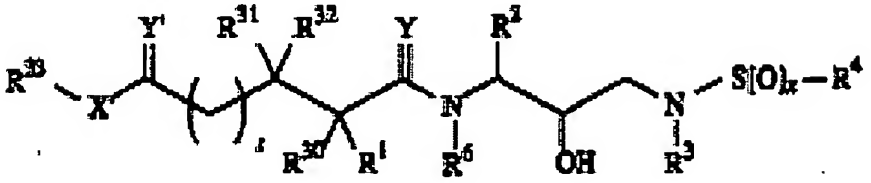
example from the prior patent would be  , which is [1S-[1R*(S*), 2S*]]-4-[[2-hydroxy-3-[(2-methylpropyl)(phenylsulfonyl)amino]-1-(phenylmethyl)propyl] amino]-2,2,3-trimethyl-4-oxo-butanoic acid (U.S. Patent No. 5,463,104, col. 59, lines 13 - 15). This species is the same as would be obtained using the present invention where $\mathbf{R^{33}}$ and $\mathbf{R^{34}}$ are both hydrogen; **X'** is oxygen; **Y** and **Y'** are both oxygen; **x** = 2; **t** = zero; $\mathbf{R^1}$ is hydrogen; $\mathbf{R^2}$ is benzyl; $\mathbf{R^3}$ is isopentyl; $\mathbf{R^4}$ is phenyl; $\mathbf{R^6}$ is hydrogen; and $\mathbf{R^{30}}$, $\mathbf{R^{31}}$, and $\mathbf{R^{32}}$ are all methyl groups.

Claim 66 of the present application claims a "pharmaceutical composition comprising the compound of Claim 1 and a pharmaceutically acceptable carrier." Likewise, U.S. Patent 5,463,104 claims a "pharmaceutical composition comprising a compound of claim 2 and a pharmaceutically acceptable carrier." (See col. 55, lines 49 – 50).

Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the current application is that the genus structure in the prior art is broader at the "$\mathbf{R^2}$" site than the instant application. In the present application, the genus structure is  ,

while the genus structure in the prior art is:



In the prior art, R^2 has a broader definition ("alkyl, aryl, cycloaryl, cycloalkylalkyl or aralkyl radicals...") than the "phenylmethyl" group required in the instant application at that same site; however, the dependent claims in the prior art subsequently narrow the definition of R^2 to just a few substituent groups, including "benzyl" (See col. 56, line 54, Claim 7), so the prior art does teach that "benzyl" is a preferred value for R^2. The other variables (such as R^{33}, R^{34}, X', Y, Y', x, t, R^1, R^2, R^3, R^4, R^6, R^{30}, R^{31}, and R^{32}) are consistent between the prior art and the present application. [Note: R^{34} appears to be inadvertently omitted from the drawing of the genus structure in the prior art, even though R^{34} is defined in the claim itself at col. 54, line 38 and is disclosed in the Specification].

Likewise, **Claim 66** ("pharmaceutical composition") in the present application is the same invention as the corresponding claim in U.S. Patent 5,463,104, inasmuch as each claims the "composition of [the corresponding] compound" and a "pharmaceutically acceptable carrier."

Resolving the level of ordinary skill in the pertinent art

The substitution of a "benzyl" group at R^2 in the prior art would have been obvious to a person of skill in the art at the time of the application, because the subsequent dependent claims teach toward "benzyl" at R^2, and each of the fifteen chemical compounds specifically claimed in the prior art use a benzyl group ("phenylmethyl") at that site. (See Claim 14, col. 58, line 61 – col. 59, line 47). The claimed uses (inhibitors of HIV protease) of the inventions are exactly the

same. A person of skill in the art would be motivated to select a "benzyl" group at the R^2 position, given the claims of U.S. Patent No. 5,463,104 showing 15 species with that substituent to be inhibitors of HIV protease.

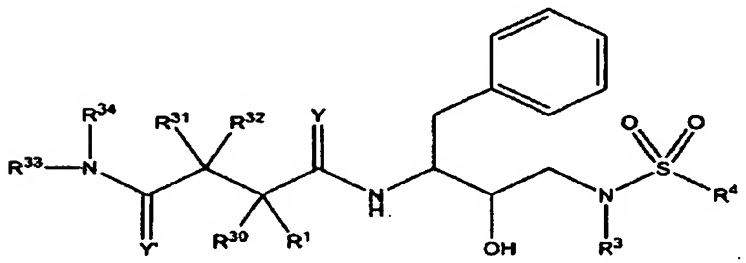
In the same way, it would have been obvious to a person of skill in the art at the time of the application to combine the compounds claimed in Claim 14 (of the prior art) with a pharmaceutically acceptable carrier to create a "pharmaceutical composition." The person of skill in the art would have been motivated to combine the compound and a carrier because the composition had already been claimed in U.S. Patent No. 5,463,104 (See Claim 3, col. 55).

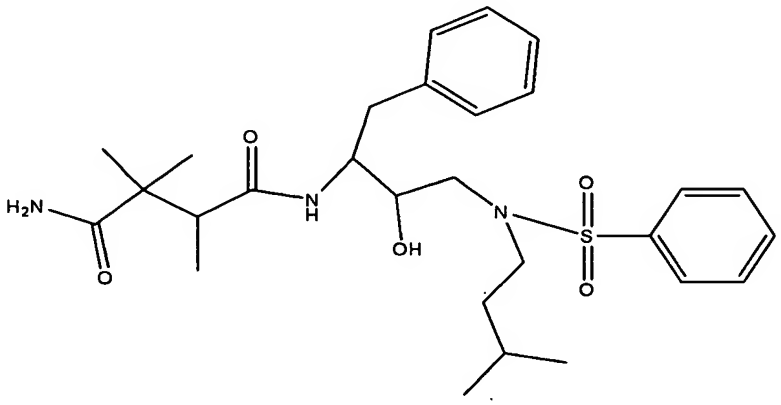
Double patenting – Claims 78 and 126:

Claim 78 (compound) and **Claim 126** (composition of compound of Claim 78 and a carrier) of the instant application are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 8, 9, 10, 11, 12, 13 and 14 of U.S. Patent No. 5,463,104. The prior patent was issued to the same inventors and assignee as the present application. Although the conflicting claims are not identical, they are not patentably distinct from each other because the chemical compounds claimed in U.S. Patent No. 5,463,104 fully encompass the compounds/compositions in **Claims 78** and **126** of the present application.

Determining the scope and content of the prior art

Claim 78 of the present application discloses compounds of the following structure:



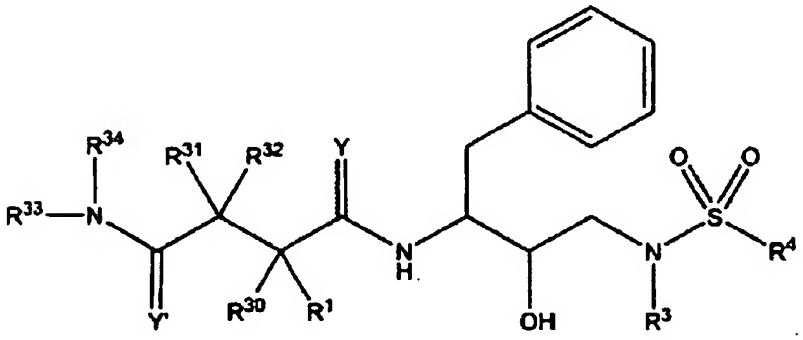
U.S. Patent No. 5,463,104 claims five chemical compounds which fully anticipate the genus structure in **Claim 78** of the present application. (See "Claim 14" of U.S. Patent No. 5,463,104, col. 59, lines 62 – 64, and col. 59, lines 6 – 8, 16 – 18, and 33 – 39). An example from the prior patent would be  , which is N^4-[2-hydroxy-3-[(3-methylbutyl)-(phenylsulfonyl)amino]-1-(phenylmethyl)propyl]-2,2,3-trimethyl-butanediamide (U.S. Patent No. 5,463,104, col. 58, lines 62 - 64). In this example, the species from the prior art would be the same as the generic structure in the present application if the following substitutions were made: $\mathbf{R^{33}}$ and $\mathbf{R^{34}}$ are both hydrogen; **Y** and **Y'** are both oxygen; **x** = 2; **t** = zero; $\mathbf{R^1}$ is hydrogen; $\mathbf{R^2}$ is benzyl; $\mathbf{R^3}$ is isopentyl; $\mathbf{R^4}$ is phenyl; $\mathbf{R^6}$ is hydrogen; and $\mathbf{R^{30}}$, $\mathbf{R^{31}}$, and $\mathbf{R^{32}}$ are each methyl groups.

Claim 126 of the present application claims a "pharmaceutical composition comprising the compound of Claim 78 and a pharmaceutically acceptable carrier." Likewise, U.S. Patent 5,463,104 claims a "pharmaceutical composition comprising a compound of claim 8 and a pharmaceutically acceptable carrier." (See col. 57, lines 47 – 48).

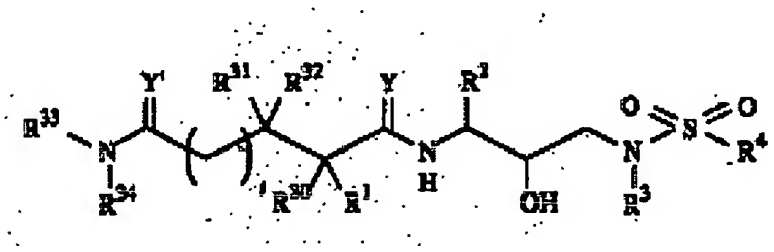
Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the current application is that the genus structure in the prior art is broader at the "$\mathbf{R^2}$" site than the instant application, and **t** represents 0 or 1 in the prior art, but only represents zero in the present application.

Specifically, in the present application, the genus structure is



, while the genus structure in the prior art is



In the prior art, $\mathbf{R^2}$ has a broader definition ("alkyl, aryl, cycloaryl, cycloalkylalkyl or aralkyl radicals...") than the "phenylmethyl" group required in the instant application, although the dependent claims in the prior art subsequently narrow the definition of $\mathbf{R^2}$ to just a few substituent groups, including "benzyl" (See col. 58, lines 46-47, Claim 13). In the same way, the values for "**t**" are narrowed to "**t** is 0 [zero]" (See, e.g., col. 58, lines 7, 25, and 42). The other variables are consistent between the prior art and the present application [note: as before, $\mathbf{R^{34}}$ appears to be inadvertently omitted from the drawing of the genus structure of the prior art, even though $\mathbf{R^{34}}$ is defined in the claim itself at col. 54, line 38 and is disclosed in the Specification].

Claim 126 (composition) in the present application is the same invention as the corresponding claim in the prior art, inasmuch as each claims the composition of the corresponding compound and a pharmaceutically acceptable carrier.

Resolving the level of ordinary skill in the pertinent art

The substitution of a "benzyl" group at $\mathbf{R^2}$ in the prior art would have been obvious to a person of skill in the art at the time of the application, because the subsequent dependent claims teach toward "benzyl" at $\mathbf{R^2}$, and each of the fifteen chemical compounds specifically claimed in the prior art use a benzyl group ("phenylmethyl") at that site. (See Claim 14, col. 58, line 61 – col. 59, line 47). Likewise, it would have been obvious to a person of skill in the art to make a compound where **t** = 0, as this is taught in subsequent dependent claims (See, e.g., col. 58, lines 7, 25, and 42). The claimed uses (inhibitors of HIV protease) of the inventions are exactly the same. A person of skill in the art would be motivated to use a benzyl group at $\mathbf{R^2}$ and t = zero, given the claims of U.S. Patent No. 5,463,104 showing these compounds to be inhibitors of HIV protease.

In the same way, it would have been obvious to a person of skill in the art at the time of the application to combine the five "butanediamide" compounds claimed in Claim 14 (of the prior art) with a pharmaceutically acceptable carrier to create a pharmaceutical composition. The person of skill in the art would have been motivated to do so because the composition had already been taught and claimed in U.S. Patent No. 5,463,104 (See col. 57, Claim 9).

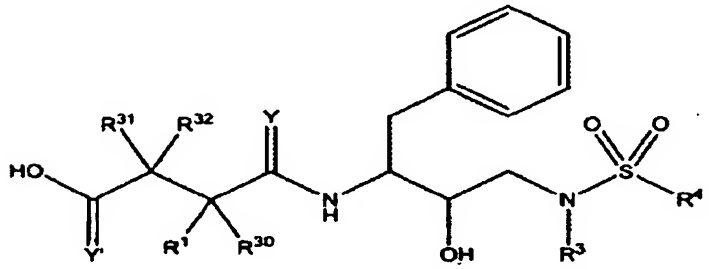
Double patenting – Claims 132 and 167:

Claim 132 (compound) and **Claim 167** (composition of compound of Claim 132 and a carrier) of the instant application are rejected under the judicially created doctrine of

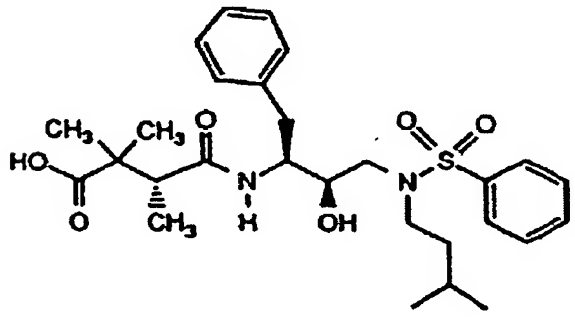
obviousness-type double patenting as being unpatentable over Claims 16, 17, 18, 19, 20 and 21 of U.S. Patent No. 5,463,104. The prior patent was issued to the same inventors and assignee as the present application. Although the conflicting claims are not identical, they are not patentably distinct from each other because the chemical compounds claimed in U.S. Patent No. 5,463,104 fully encompass the compounds/compositions in **Claims 132 and 167** of the present application.

Determining the scope and content of the prior art

Claim 132 of the present application discloses compounds of the following structure:



U.S. Patent No. 5,463,104 claims five chemical compounds which fully anticipate the genus structure in **Claim 132** of the present application. (See "Claim 14" of U.S. Patent No. 5,463,104, col. 59, lines 2 – 5, lines 13 – 15, 23 - 25, and 44 – 46). An example would be [1S-[1R*(S*),2S*]]-4-[[2-hydroxy-3-[(3-methylbutyl) (phenylsulfonyl)amino]-1-(phenylmethyl) propyl]amino]-2,2,3-trimethyl-4-oxo-butanoic acid, which has the structure:

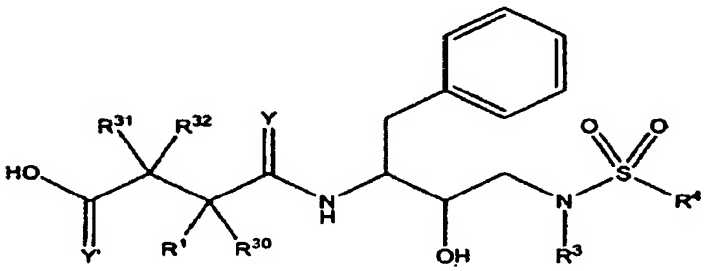
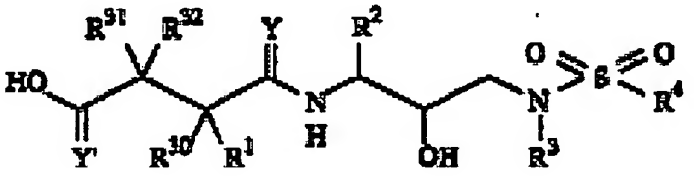


. Another example would be [1S-[1R*(S*), 2S*]]-

4-[[2-hydroxy-3-[(2-methylpropyl)(phenylsulfonyl)amino]-1-(phenylmethyl)propyl] amino]-2,2,3-trimethyl-4-oxo-butanoic acid (U.S. Patent No. 5,463,104, col. 59, lines 13 - 15).

Claim 167 of the present application claims a "pharmaceutical composition comprising the compound of Claim 132 and a pharmaceutically acceptable carrier." Likewise, U.S. Patent 5,463,104 claims a "pharmaceutical composition comprising a compound of claim 16 and a pharmaceutically acceptable carrier." (See col. 62, lines 27– 28).

Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the current application is that the genus structure in the prior art is broader at the "$\mathbf{R^2}$" site than the instant application. In the present application, the genus structure is  , while the genus structure in the prior art is  .

In the prior art, $\mathbf{R^2}$ has a broader definition ("alkyl, aryl, cycloaryl, cycloalkylalkyl or aralkyl radicals...") than the "phenylmethyl" group required in the instant application, although the dependent claims in the prior art subsequently narrow the definition of $\mathbf{R^2}$ to just a few substituent groups, including "benzyl" (See col. 62, line 13, Claim 20). The other variables are consistent between the prior art and the present application.

Claim 167 (composition) in the present application is the same invention as the corresponding claim in the prior art, inasmuch as each claims the composition of the corresponding compound and a pharmaceutically acceptable carrier.

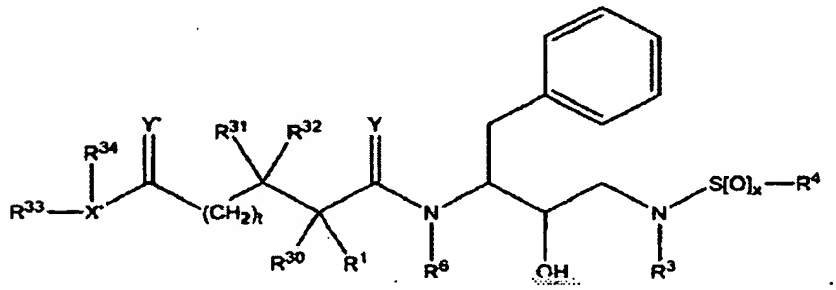
Resolving the level of ordinary skill in the pertinent art

The substitution of a "benzyl" group at $\mathbf{R^2}$ in the prior art would have been obvious to a person of skill in the art at the time of the application, because the subsequent dependent claims teach toward "benzyl" at $\mathbf{R^2}$, and each of the fifteen chemical compounds specifically claimed in the prior art use a benzyl group ("phenylmethyl") at that site. (See Claim 14, col. 58, line 61 – col. 59, line 47). The claimed uses (inhibitors of HIV protease) of the inventions are exactly the same. A person of skill in the art would be motivated to use a benzyl group at $\mathbf{R^2}$ given the claims of the prior art as inhibitors of HIV protease.

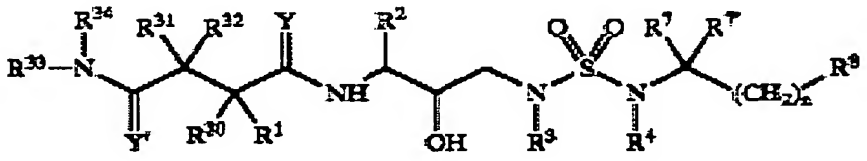
In the same way, it would have been obvious to a person of skill in the art at the time of the application to combine the compounds claimed in Claim 14 (of the prior art) with a pharmaceutically acceptable carrier to create a pharmaceutical composition. The person of skill in the art would have been motivated to do so because the composition had already been taught and claimed in the prior art (See col. 62, Claim 21).

Potential double patenting U.S. Patent No. 6,515,024 and co-pending application 10/315,254

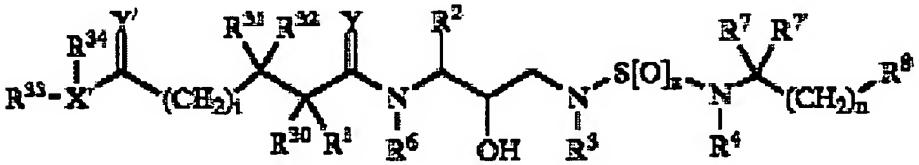
Claim 1 of the present application claims compounds of the following structure:



U.S. Patent No. 6,515,024 claims compounds of the following structure:



, and **co-pending application 10/315,254** claims compounds of the following structure:



. All three share more than one inventor, and the same assignee. All three claim the above compounds as well as the related compositions. The values can be selected in such a way that the genus claims in each would overlap (for instance, **X'** is nitrogen; **x** = 2; **t** = zero; $\mathbf{R^6}$ is hydrogen; $\mathbf{R^2}$ is benzyl; and $\mathbf{N(R^4)R^7R^{7'}(CH_2)_nR^8}$ = "di-substituted aminoalkyl radical, substituted with heteroaryl"). However, neither U.S. Patent No. 6,515,024 nor co-pending application 10/315,254 provide motivation to a person of skill in the art to select these particular values for $\mathbf{N(R^4)R^7R^{7'}(CH_2)_nR^8}$ and thus there is no obviousness-type double patenting with the claims as currently amended in the present invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Anthony J. Paviglianiti** whose telephone number is **(571) 272-3107**. The examiner can normally be reached on Monday-Friday, 8:30 a.m. - 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane, may be reached at (571) 272-0699. **The FAX phone number for the organization where this application or proceeding is assigned is (571) 273-8300. Please note that this is a new central FAX number for all official correspondence.**

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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